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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,381	02/12/2002	Evelyne Delfourne	0512-1004	3819
466	7590	02/25/2004	EXAMINER	
YOUNG & THOMPSON 745 SOUTH 23RD STREET 2ND FLOOR ARLINGTON, VA 22202			COPPINS, JANET L	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/049,381		DELFOURNE ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Janet Coppins		1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on 20 November 2003.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 7-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 11, 13 and 14 is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-10 and 12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

Claims 1-14 pending in the instant application.

#### ***Information Disclosure Statement***

1. Receipt is acknowledged of Applicants' Information Disclosure Statement (IDS), submitted June 10, 2003, which is in compliance with 37 CFR 1.97. Accordingly, the IDS has been considered by the Examiner and placed of record in the file.

#### ***Response to Amendment***

2. Receipt is acknowledged of Applicants' Amendment and Remarks, submitted November 20, 2003, which has been reviewed by the Examiner and entered of record in the file. Accordingly, claim 6 has been cancelled, and claims 1-5 and 7-14 have been amended.

#### ***Claim Rejections - 35 USC § 112***

3. Claim 12 was previously rejected under 35 USC 112, first paragraph, as not being enabled for treating all cancers. In view of the Applicants' amendatory changes to the claim, the Examiner withdraws the rejection.

#### ***Claim Rejections - 35 USC § 101***

4. The Examiner had previously rejected claims 6 and 7 for being "improper product-use" claims since they were drafted in terms of a "use." In view of the Applicants' cancellations and amendments to the claims, the 35 USC 101 rejections are obviated and the Examiner withdraws the rejections.

#### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 102***

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5. Claims 1-10 stand rejected under 35 USC 102(b) as being anticipated by Schmitz et al. Claim 13 stands rejected under 35 USC 102(b) as being anticipated by Bracher et al. Applicant's amendments to claims 1, 8, and 10, to delete hydrogen from the definition of R<sub>3</sub> obviate the aforementioned anticipation rejections. However, Applicant's arguments with respect to amended claims 1, 8, and 10 have been considered but are moot in view of the new grounds of rejection:

6. Claims 1-5 and 7-10 rejected under 35 USC 102(b) as being anticipated by Bracher, Franz "The Structure of Neocalliactine Acetate- Proof by Total Synthesis." Bracher teaches pentacyclic aromatic compounds according to formula 12 (CAS RN 143370-23-4), page 1205, which are the same as the compounds of instant formula I, wherein R<sub>3</sub> is lower alkoxy (i.e. methoxy).

### ***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-5, 7-10, and 12 rejected under 35 U.S.C. 103(a) as being unpatentable over Schmitz et al and Bracher, F.

***Applicant is claiming the following compound and processes:***

Ascididemin derivatives consisting of a pentacyclic aromatic structure, and pharmaceutical compositions containing them, methods of preparing them, and methods of using them as anti-tumor agents.

***Determination of the scope and content of the prior art (MPEP §2141.01)***

Schmitz et al teach biologically active polycyclic aromatic compounds with cytotoxic activity, isolated from marine organisms such as ascididemin, see in particular compound 2, page 1395.

Bracher also teaches polycyclic aromatic alkaloids derived from marine organisms, with cytotoxic and anti-cancer activity, please refer to compound 4a of page 59.

***Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)***

The polycyclic compounds claimed in the instant invention and the conflicting compounds of the reference articles differ in that the formulae of instant claim 1 are not identical

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to the specific compounds mentioned above, since Formula I of claim 1 recites compounds wherein a halogen may be present for R<sub>3</sub> and the remaining R substituents may be hydrogen, (i.e. the instant compounds vary by the placement of the halogen atom on the quinoline ring, which means they are positional isomers of compound 2 of Schmitz et al, which teaches a halogen on the R<sub>2</sub> position, and compound 4a of Bracher, which also teaches a halogen at the R<sub>2</sub> position).

***Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)***

To those skilled in chemical art, the instant elected group of pentacyclic aromatic alkaloid compounds is not such an advance over the genus of compounds previously published in the Schmitz et al and Bracher references, as requires invention, because chemists knowing the cytotoxic properties of the known ascididemin compounds would know what to expect in a genus of compounds that overlaps the known compounds. The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare the halo- substituted compounds, as taught in the references (i.e. as 2-bromoleptoclinidinone), with the expectation of obtaining 3-bromo substituted compounds (3- bromoleptoclinidinone) with tumor cytotoxicity. Nothing unobvious is seen in substituting the known claimed 2-bromo isomer for the structurally similar 3-bromo isomer, as taught by both Schmitz and Bracher, since such structurally related compounds suggest one another and would be expected to share common properties, absent a showing of unexpected results, please see *In re Norris*, 84 USPQ 458 (1950). It would have been prima facie obvious to employ the formulae taught in the aforementioned references, particularly when Applicants' elected compounds are taught as preferred compounds and specifically discussed in the reference articles, with a slight variation in the placement of the halogen atom. Both references also teach the methods of using the

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compounds for their anticancer activity and their cytotoxic ability against tumors. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

*Conclusion*


10. In conclusion, claims 1-5, 7-10 and 12 are rejected. Claims 11, 13, and 14 are currently free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Joseph McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins  
February 18, 2004

  
for Joseph McKane, acting SPE  
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